

The National Association of Health Underwriters is an organization of individuals involved in the sale and service of health insurance and related products. Our 16,000 members deal on a daily basis with the impact of the high cost of prescription drugs — higher health insurance premiums resulting in less access for many to comprehensive health care. Medicare beneficiaries in particular often have no purchasing assistance to help with the cost of their medications. It is a crisis that must be addressed, and we are hopeful that the United States Food and Drug Administration (FDA) will do all that is within its power to relieve the burden on consumers.

It is undisputed that the current development process of new drugs is expensive and lengthy. Only one in 10 new drugs successfully makes it to the market. Still, it is difficult for American consumers to understand the huge price disparity for identical prescription drugs in neighboring countries such as Canada and Mexico, where price controls and the ability to pay (based on average per-capita income) determine retail costs. Most Americans are now that drugs cost less in other countries, thus explaining the popularity of excursions across the border to take advantage of lower prices. To expand access to the favorable prescription drug pricing available in other parts of the world, a number of consumer advocates have called for legislation to allow reimportation of prescription drugs shipped under FDA safety guidelines to other countries. A number of logistical and safety questions about this process exist, and it again raises the question – why can't we have affordable prescription drugs here in the U.S.? Is there some way we can change the current lopsided arrangement under which U.S. citizens bear the burden for the entire cost of research and development, while other countries pay only the cost of manufacturing and little else? Do we really have to reimport our own products just to get a fair price at home? Is there anything else that can be done to give the consumer some pricing relief?

The National Association of Health Underwriters believes that one way to promote greater equity among nations and provide more affordable access to consumers would be for the FDA to convert certain prescription medications to over-the-counter status if a manufacturer is selling the drug on an over-the-counter basis in at least five developed countries, using

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appropriate standards. Exhibit 1 illustrates several common allergy medications that are sold on a prescription basis only in the U.S. but are sold over-the-counter in many other countries. These drugs, for example, have been medically proven to be safer than their current over-the-counter alternatives.

In addition to the safety issue, many consumers can't afford to consult a physician for routine allergy symptoms. To require that they do so for minor conditions that are easily self-diagnosed and treated only inflates the overall cost of medical care by encouraging unnecessary utilization of physician services. This unnecessary use combined with the inflated cost of some drugs due to their prescription only status, and greatly impacts the overall cost of health care in the U.S.

This change in FDA policy would go hand-in-hand with today's changing face of medicine. Patients are seeking greater ownership of their health care and often prefer to self-medicate when feasible. In fact, Americans are four times as likely to purchase an over-the-counter medication as they are to consult a physician. Based on recent precedent, the cost of the over-the-counter versions of many drugs is 50 percent of the prescription drug cost. Requiring patients to not only bear the higher cost of the prescription medication but also the cost of an office visit to obtain common and safe drugs places an undue time and financial burden on the patient.

In addition to modifications to FDA policy on conversion to over-the-counter status, we recommend a national education campaign on prescription drugs. NAHU believes that a strong educational initiative is critical and would be even more important if the FDA moves forward with the change of some prescription drugs to over the counter status. A strong educational initiative would assure that consumers understand the benefits and risks of specific drug products and would help consumers to use all categories of medications safely and more effectively. Consumers should be provided with accurate information on the proper use of prescription drugs, as well as safe ways to lower their costs, including the proper use of generic and over-the-counter medications. They also should be informed of that a name-brand drug might be the best treatment choice. We do not support a FDA a recommendation that consumers always purchase

generic or over the counter drugs, but we do feel that consumers should always be provided with balanced information to help them make wise purchasing decisions.

A key player in the educational process is the pharmacist. A recent study by Merck-Medco indicated that consumers rely heavily on the advice of their pharmacist, and that two out of three adults have purchased generics on the advice of their pharmacist. Current law requires pharmacists to offer consumers a choice between a name-brand drug and a generic medication when a physician has not restricted a prescription to the name-brand drug. NAHU would like to see this measure expanded so that the pharmacist would also be required to verbally advise the patient of the cost difference between their treatment choices. If the pharmacist's question is "would you like the name brand or a generic?" the implications of that choice are not as clear as if the question were "would you like the name brand for \$200 or the generic for \$68?" The majority of adults say a major reason for choosing a generic drug is **the cost differential**. Requiring similar pharmacist counseling on cost-effective over-the-counter medications would also result in significant savings for the consumer.

Finally, any consumer-education campaign should also stress the importance of lifestyle changes such as smoking cessation, low-fat diet, exercise, stress management and allergen avoidance. American reliance on a "pill for every ill," contributing to medicalization of trivial ailments and an even more overmedicated society.

NAHU believes that the rapidly escalating costs of prescription drugs poses a danger to public health that has reached crisis point. We urge the FDA to use its authority in support of the consumer and actively support over-the-counter status for safe medications, particularly those that are already sold over-the-counter in other countries.

We appreciate this opportunity to submit our comments, and welcome any questions you may have.

## Exhibit 1

*April 12, 2000*

### **FDA: 'Complex issues' require study**

#### **Decision on allergy drugs could have wide repercussions**

By Dennis Cauchon, USA TODAY

For nearly two years, the Food and Drug Administration has been reviewing whether the allergy drugs Claritin, Allegra and Zyrtec should be switched from prescription drugs to over-the-counter medicines.

The FDA, which has sole authority to decide whether drugs should be sold by prescription or over the counter, says a request made by Blue Cross of California to classify the antihistamines as over-the-counter drugs raises "complex issues."

FDA officials and industry lawyers agree that federal drug law is clear on some important points: All drugs safe enough to be sold over the counter must be made available that way. Also, the law permits anyone, from a private citizen to the FDA itself, to initiate the evaluation of whether a drug should be moved over the counter.

However, this is the first time anyone other than a drug manufacturer has made such a request.

"This hasn't been done before, and it requires a lot of study," says David Read, the FDA's acting director of regulatory policy. "Typically, the manufacturer supplies the information on a drug's safety, and we evaluate it. Now we have to ask, do we have enough information in house or has the petitioner supplied enough information for us to make a decision?"

Also at issue: Can the FDA require a manufacturer to supply safety information that could result in a drug's being moved from the lucrative prescription market to the less profitable over-the-counter market?

So far, the FDA hasn't decided any of the issues it says it is concerned about, nor has it asked Blue Cross or the drug manufacturers to address them. Blue Cross' petition, filed in July 1998, has yet to be referred to the FDA's advisory committee of outside experts that evaluates proposed over-the-counter drugs.

The FDA gives every drug a rigorous review when a medicine is approved. One reason the FDA has never initiated moving a drug over the counter is that the agency is overworked and cautious, says Raymond Woolsey, chairman of the pharmacology department at Georgetown University Medical Center in Washington.

"There's no incentive to do it," Woolsey says. "The FDA doesn't want to take the blame if something goes wrong."

The FDA also is reluctant to act because of the enormous economic consequences a decision could have on the pharmaceutical industry, says Robert Pinco, a former director of over-the-counter drugs at the FDA and now a pharmaceutical industry lawyer.

"The official (FDA) position is money doesn't matter," Pinco says. "But below the radar, they take into account the financial repercussions of their decisions. They have to take money into account. Otherwise, it would bastardize the economics underlying the pharmaceutical industry."

Insurance companies do not reimburse for over-the-counter drugs. So although the FDA cannot legally consider the economic consequences of its acts, the agency is essentially being asked to determine whether insurance companies will pay for Claritin or whether Schering-Plough, its manufacturer, must sell directly to price-sensitive consumers.

The FDA's actions on antihistamines will set a precedent that could have repercussions far beyond them. More than 40 other drugs, including many of the most popular and expensive, are candidates to be moved over the counter, according to the Consumer Healthcare Products Association, an industry trade group.

The world's top-selling drug, Prilosec, a \$3-a-pill heartburn medicine, is already being moved over the counter in other countries. Two expensive, new blockbuster painkillers, Vioxx and Celebrex, appear to have significantly fewer serious side effects than Tylenol and Motrin, popular over-the-counter painkillers.

If Blue Cross is successful in getting Claritin reclassified, it could revolutionize consumer access to the newest, safest and most effective drugs.

The FDA says it supports moving safe drugs over the counter. Since 1976, more than 600 drugs have been moved over the counter (OTC), all at the request of their manufacturers.

"If a product can be used safely by people without professional advice, it should be made available over the counter. That is a value we have," says Robert DeLap, a physician who heads over-the-counter drug review at the FDA.

"We don't take into account money. We do take into account public health," DeLap adds. "If we see that the public health is affected, we try to make the right thing happen. If we're persuaded that a product can be used appropriately and has a good safety margin, we want to make it available OTC -- indeed, we must make it available."

But he adds, "You don't want to deep-six the drug companies." That could damage research into new drugs, he says.

The FDA says it looks at three primary questions in deciding whether a drug can be sold over-the-counter:

Can the condition be adequately diagnosed by an average patient?

Can the condition be successfully treated by the average patient?

Is the product safe and effective under conditions of actual use by consumers?

The FDA already accepts allergy as an illness that can be self-diagnosed and self-treated. More than 25 antihistamines are sold over the counter.

The third question, the product's safety and effectiveness, is the key to establishing whether Claritin, Allegra and Zyrtec should be sold over the counter.

*April 12, 2000*

### **Allergy drugs remain restricted**

By Dennis Cauchon, USA TODAY

Claritin, the world's top-selling allergy drug, is sold over the counter in most industrialized countries. A month's supply costs \$13 in Australia and \$17 in Canada.

But in the United States, where Claritin is the most heavily advertised drug, it is sold only to people carrying a doctor's prescription. A month's supply costs an average of \$62.

As a result, U.S. consumers and insurers pay at least \$1.3 billion extra a year for the antihistamine, plus another \$1.3 billion for doctors' visits to get prescriptions, a USA TODAY investigation found. And because most cost-conscious Americans treat their allergies with cheaper, over-the-counter products such as Benadryl, which causes sedation, about 600 people a year lose their lives in car accidents that might have been prevented, USA TODAY estimates.

Low prices and over-the-counter access have turned a new generation of safer, non-sedating antihistamines -- Claritin, Allegra and Zyrtec -- into the primary allergy treatment in every industrialized nation except the United States.

In this country, most allergy sufferers still rely on Benadryl and other over-the-counter drugs developed a half-century ago. The recommended doses of these older antihistamines cause sedation that is the equivalent of being legally drunk, according to numerous studies in Europe and the USA. The old antihistamines have been documented by government agencies as an important cause of fatal automobile, bus and plane crashes. Studies have also shown that the same drugs impair learning and cause thousands of accidental poisonings of young children every year.

By contrast, Claritin causes no sedation and has no significant side effects. The drug is so safe that no lethal dose is known. Allegra has a similar safety record. Zyrtec causes a small amount of sedation.

Citing the new antihistamines' safety record, Blue Cross of California has asked federal regulators to move Claritin, Allegra and Zyrtec to over-the-counter status immediately.

"They advertise these drugs like they're candy," says Rob Seidman, vice president for pharmacy at Blue Cross of California, a subsidiary of WellPoint Health Networks, the nation's fourth-largest health insurer. "Claritin is one of the safest drugs in the world. The requirement to see a doctor has nothing to do with health and everything to do with marketing."

Blue Cross's petition to the Food and Drug Administration says that it is bad policy and contrary to federal law to require a doctor's prescription for such remarkably safe drugs. "Requiring that a patient schedule an office visit to obtain safe medications such as Allegra/Allegra-D, Claritin/Claritin-D or Zyrtec is an undue time and financial burden to the patient ... and trivializes the patient-physician relationship," the petition says.

The FDA, citing "complex issues," has not acted on the petition, which was filed in July 1998.

Schering-Plough Inc., which makes Claritin, has used the drug's safety record to persuade regulatory agencies in other countries to let the company sell the drug over the counter. But in the United States, Schering-Plough opposes selling Claritin over the counter, calling it unsound medical practice.

In a written response to questions from USA TODAY, the company said: "Schering-Plough believes the prescription-only status for Claritin presents the best medical option available for allergy patients."

Blue Cross' effort, if successful, could fundamentally alter the way drugs are priced and how quickly consumers get over-the-counter access to new medicines.

Schering-Plough has made billions of dollars by keeping Claritin in the lucrative U.S. prescription drug market -- and far from the fiercely price-competitive over-the-counter market. Last year, the company generated \$2.3 billion of its \$2.7 billion in worldwide revenue for Claritin in the United States. The drug is the ninth-best-selling drug in the United States and the most heavily advertised. It is Schering-Plough's top-selling product, accounting for about 30% of company revenue, according to the company's financial reports.

The marketing of Claritin, Allegra and Zyrtec as prescription drugs reveals much about why this country has the world's highest drug prices. It also illustrates how drug companies have turned laws designed to protect consumer health into shields against price competition.

Since 1951, the Food, Drug and Cosmetic Act has required that all drugs safe enough to be sold over the counter must be made available that way. The law says drugs should require a prescription only if "toxicity or other potentiality for harmful effect" makes it necessary for a doctor to supervise the patient.

But unlike regulators in other countries with similar laws, the FDA has never moved a drug to over-the-counter status -- unless a manufacturer made the request. Drug companies prefer to keep drugs in the high-priced prescription market until a drug's patent expires, when it becomes vulnerable to competition from low-priced generic prescription drugs, according to industry executives, consultants and lawyers.

This has resulted in a little-known industry practice of requiring doctors' prescriptions for newer, safer drugs while older drugs with more side effects are sold over the counter. Schering-Plough, for example, sells the sedating antihistamine Chlor-Trimeton as its low-priced, over-the-counter product while selling Claritin as its high-priced prescription drug.

For this report, USA TODAY reviewed more than 150 medical studies of antihistamines, interviewed more than a dozen allergy researchers and reviewed price and sales data from around the world. Without exception, the medical studies and medical experts agree that Claritin, Allegra and Zyrtec are significantly safer than every over-the-counter allergy treatment now sold



in the United States.

"If you put any drugs behind the counter, it should be the old antihistamines. They're the ones with all the dangerous side effects," says Gary Kay, a Georgetown University neuropsychologist who has studied the effects of antihistamines for the government and drug companies.

### **Stopping 50 million runny noses**

Fifty million people suffer from allergies in the United States.

The cause of allergies was discovered in 1907: Exposure to pollen and other allergens causes the release of a chemical called histamine, which grabs onto nerve endings and produces a runny, congested nose and watery eyes. Antihistamines are chemicals that block this process.

Swiss scientist Daniel Bovet won a Nobel Prize for finding the first effective antihistamine in 1944. The first antihistamine widely used was introduced the next year: diphenhydramine.

Today, diphenhydramine is best known as Benadryl, still the most common allergy treatment in the United States. Two dozen other antihistamines were introduced about the same time, including chlorpheniramine (Chlor-Trimeton), brompheniramine (Dimetapp) and clemastine (Tavist). Benadryl switched from prescription to over-the-counter status in 1981, Chlor-Trimeton in 1976.

The old and the new antihistamines are equally effective at controlling symptoms, but the old drugs have a big drawback: the chemicals enter the brain and affect the central nervous system. This causes a range of effects: sleepiness, slowed reactions, impaired coordination, inability to concentrate and dizziness. Rare side effects include seizures, hallucinations and death from accidental overdoses, especially in children.

Claritin, Allegra and Zyrtec don't have any of those side effects. The reason: the new antihistamines use bigger molecules that do not easily cross into the brain. Also, for reasons not fully understood, the new drugs gravitate to nerve endings in the body, not the brain.

The new antihistamines are also free from another side effect of old antihistamines: anticholinergic activity, which causes dry mouth and urine retention. This can lead to glaucoma, blurred vision, elevated blood pressure and other problems, especially in the elderly.

"I've had older men with enlarged prostates take a course of classical antihistamines, go into urinary retention and have to wear a catheter for a few days," says Thomas Nolen, an Alabama family practitioner who has written on the antihistamines. "It's not going to kill them, but it's darn uncomfortable."

The first non-sedating antihistamine, Seldane, was introduced in the United States in 1985. It was in the process of being switched to over-the-counter status in 1991 when it was linked to a rare but sometimes fatal side effect. The drug was linked to aberrations in heart rhythms, caused by a buildup of byproducts in the liver. This problem usually happened when the drug was used

at a dose higher than recommended and mixed with some other drugs.

Hoechst Marion Roussel, the drug's manufacturer at the time, reformulated the molecule in Seldane so that its residue did not collect in the liver, which had caused the problem. The new drug, Allegra, was introduced in 1996 and appears to be free of this side effect. Claritin and Zyrtec have been researched extensively for a link to this heart problem. No connection has been found.

"The over-the-counter medicines are much more dangerous than the ones we write the prescriptions for," says allergist Robert Miles, president of the American College of Allergy, Asthma and Immunology. "The first-generation antihistamines were a very blunt instrument."

### **The human costs of OTC antihistamines**

Traffic fatalities are the leading cause of deaths linked to sedating antihistamines.

Scott Wisner, a Greyhound bus driver, was scheduled to retire in June 1998. On his final drive, on June 20, he took Benadryl for a sinus problem. The 61-year-old driver apparently fell asleep at the wheel at 4:05 a.m. on the Pennsylvania Turnpike as he neared the end of his New York-to-Pittsburgh run. The bus drifted off the highway at full speed and crashed into the back of a parked truck. Seven people died, including Wisner. Sixteen were injured.

The National Transportation Safety Board ruled Jan. 5 that the sedating antihistamine and fatigue were responsible for the driver's reduced alertness, which caused the crash.

The ingredient in Benadryl was also found in the blood of the bus driver involved in a crash in New Orleans that killed 22 people on May 9, 1999. The NTSB is examining whether the antihistamine contributed to the crash .

USA TODAY estimates that sedating antihistamines cause an average of about 600 auto fatalities per year. An additional 47,750 people per year are injured in antihistamine-related crashes.

These estimates are based on studies that tested for sedating antihistamines in the blood of drivers involved in fatal accidents. Since 1992, when Claritin was introduced in the United States, nearly 5,000 people have died in wrecks caused by sedating antihistamines, USA TODAY estimates.

These death estimates are significantly lower than those Schering-Plough uses in Europe to promote the safety of Claritin . In a May 1998 news release, the company cited a study that blamed 1,500 deaths a year in Europe and 44,500 injuries on the old antihistamines. (The European Union averages 55,000 traffic deaths per year vs. 41,500 in the United States.)

Schering-Plough's news release added: "Crash probability statistics show that sedative antihistamines increase the risk of a road traffic accident by a factor of six."

"Sedating antihistamines aren't in the league of alcohol in causing highway deaths," says Richard Compton, acting director of research at the National Highway Traffic Safety Administration. "But they no doubt cause accidents, and the highways would be safer if people used non-sedating antihistamines instead."

It is illegal to drive under the influence of sedating antihistamines in 35 states, though prosecutions are rare.

European researchers have done more than 50 studies that use real-world driving tests to compare the effects of antihistamines and alcohol. They found that a single dose of Benadryl is equivalent to a blood-alcohol content of .09 -- higher than the .08 level that makes a driver legally drunk in many states. In March, a study in the *Annals of Internal Medicine* used computerized driving simulators to confirm that driving under the influence of Benadryl is similar to driving drunk.

The results are especially worrisome, researchers say, because studies show that people don't realize that they are affected and that impairment can last a full day after taking a sedating antihistamine. "People don't feel sedated, so they don't take precautions seriously," says Kay, the Georgetown psychologist. "But they're no better judges of impairment than a drunk is of drunkenness."

Sedating antihistamines are the drug found most often in the blood of pilots killed in private plane crashes. The National Transportation Safety Board reports that sedating antihistamines have been found in the blood of more than 100 pilots involved in fatal plane crashes since 1987. In a typical case, the NTSB explained a 1996 crash that killed two in Utah this way: "Probable cause: the pilot's impairment of judgment and performance due to drugs (diphenhydramine) which led to spatial disorientation and loss of aircraft control."

High altitude exaggerates the sedating effects of the old antihistamines, which is one reason the Federal Aviation Administration forbids pilots to fly under the influence of these drugs. Altitude has no influence on the effects of Claritin and Allegra, the FAA says. The agency permits pilots to use those drugs.

Sedating antihistamines have caused fatal military plane crashes and parachute mishaps, too. The Air Force grounds all pilots suffering allergy attacks. But Air Force Lt. Col. Gilbert Hansen, a physician, wrote in a study in September 1999 that "in an attempt to avoid being grounded, some pilots have chosen, despite warnings, to self-medicate with over-the-counter first-generation antihistamines. In at least one incident, this behavior led to loss of life and the destruction of hundreds of millions of dollars of equipment."

His solution: Let military pilots take Claritin. The issue is under review.

### **The economics of drug pricing**

Claritin, Allegra and Zyrtec had \$3.9 billion in U.S. sales in 1999. They accounted for nearly 4% of all prescription drug spending outside hospitals in this country. Yet only 23% of allergy

sufferers use these prescription drugs.

By contrast, 56% of allergy sufferers treat themselves with over-the-counter antihistamines. Despite dominating the market, over-the-counter antihistamines last year generated just \$325 million in sales. (The remaining 21% of allergy sufferers don't get treatment or choose to use home remedies.)

Benadryl had sales of \$148 million in the United States in 1999 and just \$9 million in the rest of the world.

Price and easy availability heavily influence consumers' choices. The average retail price of a pack of over-the-counter antihistamines is \$4.50 vs. \$62 for Claritin.

Managed-care organizations can treat allergies for as little as 3 cents a day when buying sedating antihistamines in bulk vs. \$2.03 a day for Claritin, according to a 1998 study in *Otolaryngologic Clinics of North America*.

"Schering doesn't want Claritin switched because it has wonderful profit margins now and doesn't think it could come close to that in the OTC market," says William Soller, senior vice president of the Consumer Healthcare Products Association, a trade group for over-the-counter drug makers, including Schering-Plough.

Drug companies can charge higher prices when insurers pay most of the bill.

As the spring allergy season begins, U.S. retail prices for Claritin, Allegra and Zyrtec -- already the highest in the world -- have risen slightly. By contrast, in Canada, the allergy season has brought on a price war. The Loblaw grocery store chain in Canada, for example, is having a two-for-one sale that slashes Claritin's price to less than 28 cents a pill vs. \$1.94 at discount pharmacies in the United States.

Blue Cross of California estimates that U.S. antihistamine prices would fall by half if the drugs were moved over the counter. The cost then would be roughly the same as the co-pays charged now for the drug and the required doctor's visit -- about \$27.

But industry consultant Steve Francesco says that's wishful thinking. "Blue Cross wants to stop reimbursing for Claritin, so they've created this convenient fiction about its price," Francesco says. He predicts the price of Claritin would drop only slightly unless, as Blue Cross also requested, Allegra and Zyrtec also were classified as over-the-counter drugs.

"Claritin can charge five to eight times more than Benadryl because it's a better product, but if they had to compete with Allegra, there would be a real downward pressure on price," Francesco says.

Pharmaceutical companies try to keep drugs out of the price-sensitive over-the-counter market until a drug's patent expires -- on average, 12 years after FDA approval. When a patent expires, competitors enter the market, offering the same drug for an average of 73% less than the original

price.

It is at this point that drug companies typically ask the FDA to move a drug over the counter. Drug companies can win three additional years of exclusivity if the FDA rules that that new studies, paid for by the manufacturer, are essential for over-the-counter approval.

High prices charged during the years a drug is patented determine a drug's profitability and whether a company recovers the \$313 million it costs, on average, to bring a drug to market.

Robert Pinco, a former director of over-the-counter drugs at the FDA, says the Blue Cross petition puts the FDA and Schering-Plough in difficult positions. By law, the FDA can consider only medical issues, although what's really at stake is the drug's profitability, he says. Schering-Plough's case is further hurt because the company has argued in other countries that the drug is safe enough to be sold over the counter, he says.

"It's a clever way for Blue Cross to try to save money. If it goes through, it might benefit consumers in the short term, but it's going to devastate the bottom line of pioneer drug companies," Pinco says.

"The FDA is befuddled," says Soller, the executive at the over-the-counter drug trade group. "The law says anybody can force a switch. You or I could do it. But it's always been left to the manufacturers, so if this goes through, the fluff will hit the fan."

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## The prices of pills

Daily costs of nonsedating antihistamines in selected countries in U.S. dollars:

Drug	Manufacturer	USA	Canada	England	New Zealand	Australia	Mexico	Poland
Claritin	Schering-Plough	\$1.94	\$0.57	\$0.96	\$0.67	\$0.43	\$0.93	\$0.44
Allegra	Aventis	\$1.76	\$0.60	\$0.92	\$0.78	\$0.44	\$0.95	NS*
Zytec	Pfizer-UCB	\$1.62	\$0.56	\$0.96	\$0.58	\$0.44	\$0.90	\$0.20

Source: USA TODAY research, \* not sold in Poland.